

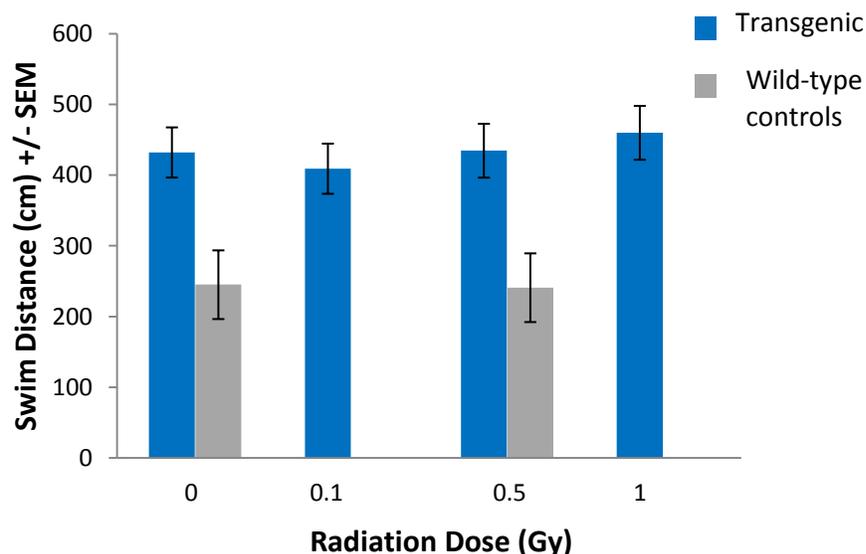
## Low Doses of Proton Radiation do not Induce Spatial Learning or Memory Deficits in a Mouse Model of Alzheimer's Disease

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Astronauts traveling outside Earth's magnetosphere risk exposure to charged particle radiation that has been shown to cause neurological deficits at high doses. The hippocampus has been identified as a particularly susceptible structure, with exposure resulting in oxidative stress, synaptic changes, reduced neurogenesis and neuroinflammation. However, the neurodegenerative effects of low doses of radiation are not well understood, and it is unknown whether individuals with a propensity toward developing Alzheimer's disease (AD) are more adversely affected. In the present study, we exposed young transgenic APP/PSEN1 mice (a strain engineered to develop age-related AD-like neuropathology) and their wild-type littermates to different doses of proton particle radiation to assess the effects on hippocampus-dependent behaviors. Spatial learning ability, which is particularly vulnerable to hippocampal damage, was assessed using the water maze 3 and 6 months after irradiation (Barnes maze data were also attained, but are still in the process of being analyzed). Transgenic mice were found to have greater behavioral deficits than the wild-type mice, as evidenced by the longer swim path required to find the hidden platform. However, radiation doses up to 1 Gy had no effect on performance. These findings suggest that low doses of proton radiation do not increase the risk of developing learning and memory deficits even in those individuals predisposed toward age-related neurological diseases.

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**6 month behavioral outcome by dose/genotype:** The wild-type mice had a more direct path to the hidden platform than the transgenic (APP/PSEN1) mice. No radiation-induced differences were found among the transgenic animals.